

EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|-------|------|-----------------------|---|------------------|---------|------------------|
| L1 | 991 | merkulov.in. | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:14 |
| L2 | 123 | L1 same gennady | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:14 |
| L3 | 90 | L2 same V | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:15 |
| L4 | 858 | Ketchum.in. | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:15 |
| L5 | 292 | L4 same karen | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:15 |
| L6 | 267 | L5 same A | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:15 |
| L7 | 2812 | L4 (karen adj A) | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:15 |
| L8 | 267 | L4 same (karen adj A) | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:16 |
| L9 | 248 | L8 and antibod\$ | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:16 |

EAST Search History

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|-----|------|--|---|----|----|------------------|
| L10 | 856 | (Di adj Francesco).in. | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:17 |
| L11 | 531 | L10 same valentina | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:16 |
| L12 | 0 | (Valentina adj Di adj Francesco).in. | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:17 |
| L13 | 0 | (Valentina adj (Di adj Francesco)).in. | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:17 |
| L14 | 2172 | Beasley.in. | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:17 |
| L15 | 606 | L14 same (ellen adj M) | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:18 |
| L16 | 548 | L15 and antibod\$ | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:18 |
| L17 | 14 | L15 and lipase\$ | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:18 |
| L18 | 7 | L9 and lipase | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | OR | ON | 2006/12/21 20:18 |

FILE 'CAPLUS' ENTERED AT 20:19:27 ON 21 DEC 2006

E MERKULOV V GENNADY/AU 25

L1 20 S (E2)

E KETCHUM A KAREN/AU 25

L2 19 S (E49)

E DI FRANCESCO V/AU 25

L3 8 S (E3)

E BEASLEY ELLEN/AU 25

L4 8 S (E3)

<!--StartFragment-->RESULT 6

AAU98539

ID AAU98539 standard; protein; 427 AA.

XX

AC AAU98539;

XX

DT 21-AUG-2002 (first entry)

XX

DE Human lysosomal acid lipase protein #2.

XX

KW Human; lysosomal acid lipase; cancer; CNS; obesity; chromosome 10;
KW central nervous system disorder; chronic obstructive pulmonary disease;
KW diabetes; cardiovascular disorder; Alzheimer's disease; dementia;
KW Parkinson's disease; multiple sclerosis; Huntington's disease; pain;
KW congestive heart failure; myocardial infarction.

XX

OS Homo sapiens.

XX

PN WO200236754-A2.

XX

PD 10-MAY-2002.

XX

PF 26-OCT-2001; 2001WO-EP012382.

XX

PR 31-OCT-2000; 2000US-0244215P.

PR 06-DEC-2000; 2000US-0251401P.

XX

PA (FARB) BAYER AG.

XX

PI Xiao Y;

XX

DR WPI; 2002-490007/52.

DR N-PSDB; ABK85978.

XX

PT Novel human lysosomal acid lipase polypeptide, useful for treating
PT cancer, central nervous system disorder, obesity, chronic obstructive
PT pulmonary disease, diabetes or cardiovascular disorder.

XX

PS Claim 1; Fig 5; 126pp; English.

XX

CC This invention relates to the DNA and protein sequences of a purified
CC human lysosomal acid lipase protein. The sequences of the invention are
CC useful for screening for agents which modulate the activity of human
CC lysosomal acid lipase polypeptide. A compound which increases human
CC lysosomal acid lipase activity may be identified as a potential
CC therapeutic agent for increasing the activity of the human lysosomal acid
CC lipase, and a test compound which decreases the human lysosomal acid
CC lipase activity is identified as a potential therapeutic agent for
CC decreasing the activity of human lysosomal acid lipase. A pharmaceutical
CC compound containing the lysosomal acid lipase sequences is useful for the
CC preparation of a medicament for modulating the activity of human
CC lysosomal acid lipase in a disease such as cancer, central nervous system
CC (CNS) disorder, obesity, chronic obstructive pulmonary disease, diabetes
CC or a cardiovascular disorder. A reagent that modifies the activity of the
CC protein of the invention is useful for treating a human lysosomal acid
CC lipase dysfunction related disease, preferably the above mentioned
CC diseases. A DNA or protein sequence of the invention is useful for
CC treating the above mentioned disorders, where the CNS disorders are
CC selected from Alzheimer's and Parkinson's disease, dementia, multiple
CC sclerosis, Huntington's disease, and pain, and the cardiovascular
CC disorder is selected from congestive heart failure and myocardial

CC infarction. The present sequence represents a human lysosomal acid lipase
CC protein of the invention, the gene encoding this protein is located on
CC human chromosome 10
XX
SQ Sequence 427 AA;

Query Match 95.0%; Score 2030; DB 5; Length 427;
Best Local Similarity 97.2%; Pred. No. 2.3e-195;
Matches 379; Conservative 2; Mismatches 7; Indels 2; Gaps 2;

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Qy      1 MMWLLLT'T'CLICGTLNAGGFLDLENEVNPEVWMNTSEIIIIYNGYPSEEYEVTTTEDGYIL 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      30 MMWLLLT'T'CLICGTLNAGGFLDLENEVNPEVWMNTSEIIIIYNGYPSEEYEVTTTEDGYIL 89

Qy     61 LVNRIPYGRTHARSTGPRPVVYMQHALFADNAYWLENYANGSLGFLLADAGYDVWMGNSR 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     90 LVNRIPYGRTHARSTGPRPVVYMQHALFADNAYWLENYANGSLGFLLADAGYDVWMGNSR 149

Qy    121 GNTWSRRHKTLSETDEKFWAFSFDDEMAKYDLPGVIDFIVNKTGQEKLYFIGHSLGTTIGF 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    150 GNTWSRRHKTLSETDEKFWAFSFDDEMAKYDLPGVIDFIVNKTGQEKLYFIGHSLGTTIGF 209

Qy    181 VAFSTMPELAQRIKMNFALGPTISFKYPTGIFTRFFLLPNSIIKAVFGTKGFFLEDKGTK 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    210 VAFSTMPELAQRIKMNFALGPTISFKYPTGIFTRFFLLPNSIIKAVFGTKGFFLEDKGTK 269

Qy    241 IASTKICNNKILWLICSEFMSLWAGSNKKNMNQSRMDVYMSHAPTGSSVHNILHIKQLYH 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    270 IASTKICNNKILWLICSEFMSLWAGSNKKNMNQSRMDVYMSHAPTGSSVHNILHIKQLYH 329

Qy    301 SDEFRAWDGNDADNMKHYNQSHPPPIYDLTAMKVPTAIWAGGHDVLGTPQDVARILPQIK 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    330 SDEFRAWDGNDADNMKHYNQSHPPPIYDLTAMKVPTAIWAGGHDVLVTPQDVARILPQIK 389

Qy    361 SLSLVLSLLPEWEPTFDFVWGLDAPQRMFS 390
      ||   |||:|   |||||||||||||:|
Db    390 SLH-YFKLLPDWN-HFDFVWGLDAPQRMYS 417
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<!--EndFragment-->

<!--StartFragment-->RESULT 3

LICH_HUMAN

103

ID LICH_HUMAN STANDARD; PRT; 399 AA.
AC P38571; Q16529; Q96EJ0;
DT 01-OCT-1994, integrated into UniProtKB/Swiss-Prot.
DT 21-JUN-2005, sequence version 2.
DT 07-MAR-2006, entry version 55.
DE Lysosomal acid lipase/cholesteryl ester hydrolase precursor
DE (EC 3.1.1.13) (LAL) (Acid cholesteryl ester hydrolase) (Sterol
DE esterase) (Lipase A) (Cholesteryl esterase).
GN Name=LIPA;
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC Homo.
OX NCBI_TaxID=9606;
RN [1]
RP NUCLEOTIDE SEQUENCE, PROTEIN SEQUENCE OF 196-212; 277-297 AND 305-315,
RP AND VARIANT PRO-16.
RX MEDLINE=92042192; PubMed=1718995;
RA Anderson R.A., Sando G.N.;
RT "Cloning and expression of cDNA encoding human lysosomal acid
RT lipase/cholesteryl ester hydrolase. Similarities to gastric and
RT lingual lipases.";
RL J. Biol. Chem. 266:22479-22484(1991).
RN [2]
RP NUCLEOTIDE SEQUENCE.
RC TISSUE=Liver;
RX MEDLINE=94155897; PubMed=8112342;
RA Ameis D., Merkel M., Eckerskorn C., Greten H.;
RT "Purification, characterization and molecular cloning of human hepatic
RT lysosomal acid lipase.";
RL Eur. J. Biochem. 219:905-914(1994).
RN [3]
RP NUCLEOTIDE SEQUENCE.
RC TISSUE=Liver;
RX MEDLINE=96363957; PubMed=8725147;
RA Du H., Witte D.P., Grabowski G.A.;
RT "Tissue and cellular specific expression of murine lysosomal acid
RT lipase mRNA and protein.";
RL J. Lipid Res. 37:937-949(1996).
RN [4]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA], AND VARIANT PRO-16.
RC TISSUE=Placenta;
RX MEDLINE=22388257; PubMed=12477932; DOI=10.1073/pnas.242603899;
RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,
RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,

RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
 RT "Generation and initial analysis of more than 15,000 full-length human
 RT and mouse cDNA sequences.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
 RN [5]
 RP VARIANT CESD/WD PRO-200.
 RX MEDLINE=94195814; PubMed=8146180;
 RA Anderson R.A., Byrum R.S., Coates P.M., Sando G.N.;
 RT "Mutations at the lysosomal acid cholesteryl ester hydrolase gene
 RT locus in Wolman disease.";
 RL Proc. Natl. Acad. Sci. U.S.A. 91:2718-2722(1994).
 RN [6]
 RP VARIANTS CESD ARG-129 AND PRO-129.
 RX MEDLINE=98295576; PubMed=9633819;
 RX DOI=10.1002/(SICI)1098-1004(1998)12:1<44::AID-HUMU7>3.3.CO;2-F;
 RA Ries S., Buechler C., Schindler G., Aslanidis C., Ameis D., Gasche C.,
 RA Jung N., Schambach A., Fehringer P., Vanier M.T., Belli D.C.,
 RA Greten H., Schmitz G.;
 RT "Different missense mutations in histidine-108 of lysosomal acid
 RT lipase cause cholesteryl ester storage disease in unrelated compound
 RT heterozygous and hemizygous individuals.";
 RL Hum. Mutat. 12:44-51(1998).
 CC -!- FUNCTION: Crucial for the intracellular hydrolysis of cholesteryl
 CC esters and triglycerides that have been internalized via receptor-
 CC mediated endocytosis of lipoprotein particles. Important in
 CC mediating the effect of LDL (low density lipoprotein) uptake on
 CC suppression of hydroxymethylglutaryl-CoA reductase and activation
 CC of endogenous cellular cholesteryl ester formation.
 CC -!- CATALYTIC ACTIVITY: A sterol ester + H(2)O = a sterol + a fatty
 CC acid.
 CC -!- SUBCELLULAR LOCATION: Lysosome.
 CC -!- DISEASE: Defects in LIPA are the cause of Wolman disease (WD)
 CC [MIM:278000]. WD is a severe manifestation of LIPA deficiency,
 CC leading to the accumulation of cholesteryl esters and
 CC triglycerides in most tissues of the body. WD occurs in infancy
 CC and is nearly always fatal before the age of 1 year.
 CC -!- DISEASE: Defects in LIPA are the cause of cholesteryl ester
 CC storage disease (CESD) [MIM:278000]. CESD is a mild manifestation
 CC of LIPA deficiency, leading to the accumulation of cholesteryl
 CC esters and triglycerides in most tissues of the body. It is
 CC characterized by late-onset.
 CC -!- SIMILARITY: Belongs to the AB hydrolase superfamily. Lipase
 CC family.
 CC -----
 CC Copyrighted by the UniProt Consortium, see <http://www.uniprot.org/terms>
 CC Distributed under the Creative Commons Attribution-NoDerivs License
 CC -----
 DR EMBL; M74775; AAA59519.1; -; mRNA.
 DR EMBL; U04285; AAB60327.1; -; Unassigned_DNA.
 DR EMBL; U04286; AAB60327.1; JOINED; Unassigned_DNA.
 DR EMBL; U04287; AAB60327.1; JOINED; Unassigned_DNA.
 DR EMBL; U04288; AAB60327.1; JOINED; Unassigned_DNA.
 DR EMBL; U04290; AAB60327.1; JOINED; Unassigned_DNA.
 DR EMBL; U04291; AAB60327.1; JOINED; Unassigned_DNA.
 DR EMBL; U04292; AAB60327.1; JOINED; Unassigned_DNA.
 DR EMBL; U04293; AAB60327.1; JOINED; Unassigned_DNA.
 DR EMBL; X76488; CAA54026.1; -; mRNA.
 DR EMBL; Z31690; CAA83495.1; -; mRNA.
 DR EMBL; U08464; AAB60328.1; -; mRNA.
 DR EMBL; BC012287; AAH12287.1; -; mRNA.
 DR PIR; S41408; S41408.

Qy 242 ASTKICNNKILWLICSEFMSLWAGSNKKNMNQRSMDVYMSHAPTGSSVHNILHIKQLYHS 301
| : | : | | : | | | : : | | : | | : : | | : | |
Db 243 LGTHVCTHVILKELCGNLCFLLCGFNERNLNMSRVDVYTTTHSPACTSVQNMLHWSQAVKF 302

Qy 302 DEFRAYDWGNDADNMKHYNQSHPPYDLTAMKVPTAIWAGGHDVLGTPQDVARILPQIKS 361
: : : : | | : | | | : | | : : | | | : : | | | :
Db 303 QKFQAFDWGSSAKNYFHYNQSYPPTYNVKDMLVPTAVWSGGHDWLADVYDVNILLTQITN 362

Qy 362 LSLVLSLLPEWEPTFDFVWGLDAPQRMFSGNHNL 395
| : | | | : | : | | | | : : : | |
Db 363 LVFHES-IPEWE-HLDFIWGLDAPWRLYNKIINL 394

<!--EndFragment-->